

**S6 Fig.** Free energy profiles for two coldspots and two hotspots with G/T pair where we used set C for calculation of RMSD. At 1.55 Å the free energy for AGGTA, TGGAA, AAGAA and CAGTG is 19.5, 18.7, 17.9, and 17.5 kcal mol-1, respectively.